

=> fil reg

FILE 'REGISTRY' ENTERED AT 10:28:16 ON 15 JAN 2005  
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Property values tagged with IC are from the ZIC/VINITI data file  
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STRUCTURE FILE UPDATES: 12 JAN 2005 HIGHEST RN 812631-13-3  
DICTIONARY FILE UPDATES: 12 JAN 2005 HIGHEST RN 812631-13-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

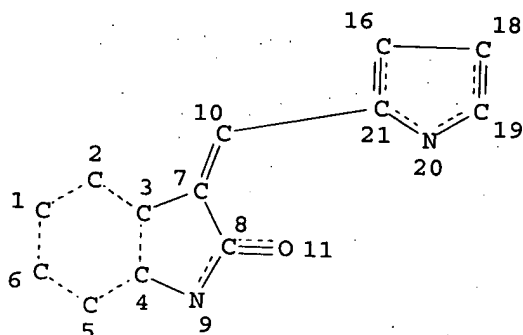
Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que 128

L20 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

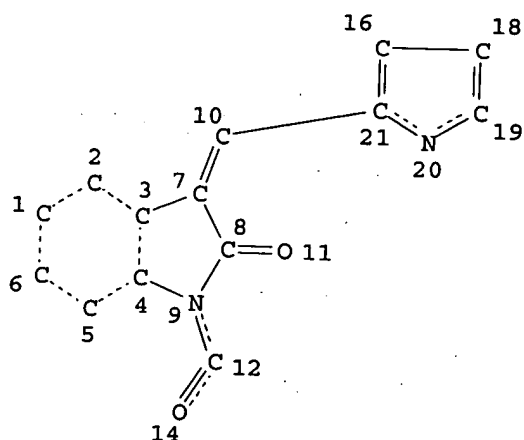
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L22 2680 SEA FILE=REGISTRY SSS FUL L20

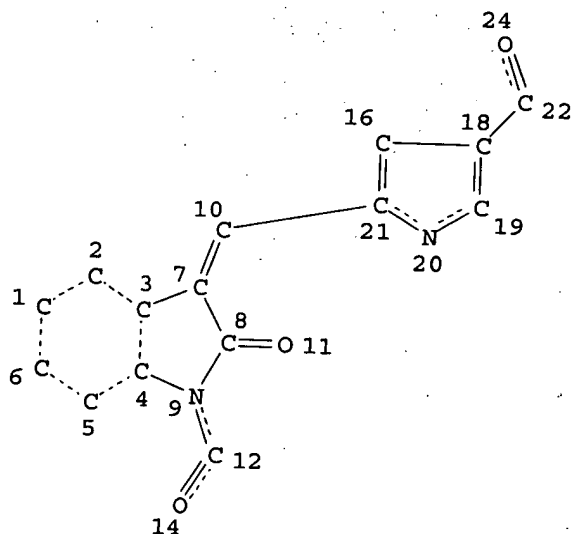
L23 STR



NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE  
 L25 48 SEA FILE=REGISTRY SUB=L22 SSS FUL L23  
 L26 STR



NODE ATTRIBUTES:  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE  
 L28 0 SEA FILE=REGISTRY SUB=L25 SSS FUL L26

100.0% PROCESSED

0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

=&gt; =&gt; fil marpat

FILE 'MARPAT' ENTERED AT 10:31:10 ON 15 JAN 2005  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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FILE CONTENT: 1988-PRESENT (VOL 142 ISS 01) (20050107/ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

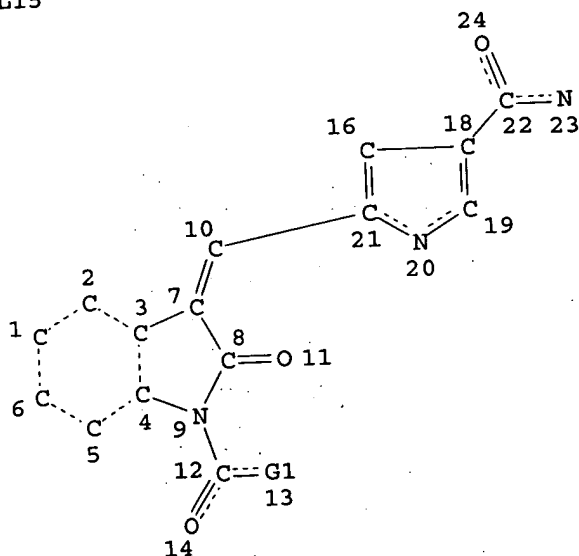
US 6806291 19 OCT 2004  
DE 10316402 21 OCT 2004  
EP 1471568 27 OCT 2004  
JP 2004300045 14 NOV 2004  
WO 2004101522 25 NOV 2004

Structure search limits have been raised. See HELP SLIMIT for the new,  
higher limits.

=&gt; d sta que

L15

STR



VAR G1=O/15

NODE ATTRIBUTES:

NSPEC IS RC AT 15

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

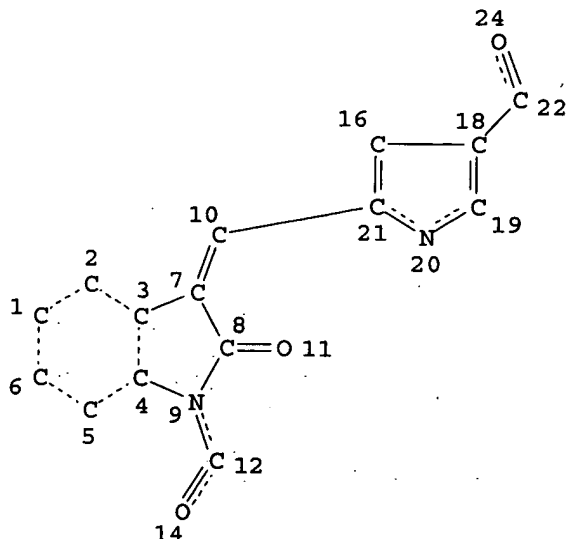
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

L26

STR



## NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

## GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 20

## STEREO ATTRIBUTES: NONE

L30 8 SEA FILE=MARPAT SSS FUL L26

L31 4 SEA FILE=MARPAT SUB=L30 SSS FUL L15

100.0% PROCESSED 8 ITERATIONS

SEARCH TIME: 00.00.01

4 ANSWERS

=&gt; =&gt; d bib abs qhit retable tot l31

L31 ANSWER 1 OF 4 MARPAT COPYRIGHT 2005 ACS on STN

AN 138:4517 MARPAT

TI Preparation of 3-heteroarylmethylidene-2-indolinone protein kinase inhibitors for use against cancer and other disorders

IN McMahon, Gerald; Tang, Peng Cho; Sun, Li

PA Sugen, Inc., USA

SO U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 74,621.

CODEN: USXXAM

DT Patent

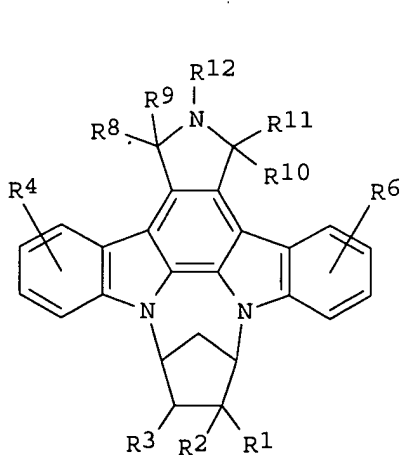
LA English

FAN.CNT 3

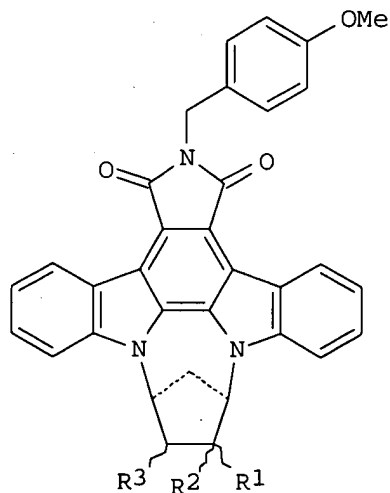
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6486185	B1	20021126	US 1998-191458	19981112
	US 6316429	B1	20011113	US 1998-74621	19980507
	US 2002156083	A1	20021024	US 2001-819698	20010329
	US 6683082	B2	20040127		
	US 2004106630	A1	20040603	US 2003-725079	20031202
	US 2004106618	A1	20040603	US 2003-725267	20031202
PRAI	US 1997-45838P		19970507		
	US 1997-59677P		19970919		
	US 1998-74621		19980507		

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:467897 CAPLUS  
 DOCUMENT NUMBER: 141:38635  
 TITLE: Preparation of N,N-bridged, nitrogen-substituted carbacyclic indolocarbazoles for use in pharmaceutical compositions as protein kinase inhibitors  
 INVENTOR(S): Monse, Barbara; Braxmeier, Tobias; Ferrand, Sandrine; Gordon, Sandra; Klafki, Hans; Lahu, Gezim; Roder, Hanno; Sahagun-Krause, Heidi; Seneci, Pierfausto; Thillaye du Boullay, Olivier  
 PATENT ASSIGNEE(S): Nad A.-G., Germany  
 SOURCE: PCT Int. Appl., 89 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048384	A1	20040610	WO 2003-EP13322	20031126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10255343	A1	20040617	DE 2002-10255343	20021127
PRIORITY APPLN. INFO.:			DE 2002-10255343	A 20021127
OTHER SOURCE(S):			MARPAT 141:38635	
GI				



I



II

AB This invention relates to the preparation of novel carbacyclic indolocarbazoles, such as I [R1 = NR13R14; R2 = H, CN, alkyl, aryl, heteroaryl, acyl, carboxy, carboxamido; R1R2 = spiro nitrogen containing heterocycle, such as spirohydantoyl; R3 = H, OR13, OCOR13, OCONHR13, OCONR13R14; R1R3 = fused heterocycle, such as -OSO2O-, and R2 = H; R4, R6 = H, CN, halogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, alkoxy, acyl,

carboxy, carboxamido, etc.; R8R9, R10R11 = H2, O, S; R8 = H, R9 = OH; R10 = H, R11 = OH; R12 = H, alkyl, cycloalkyl, benzyl aryl heteroaryl, acyl, carboxy, etc.; R13, R14 = H, alkyl, cycloalkyl, acyl, aryl, etc.], for therapeutic use as **protein kinase** inhibitors with advantageous pharmaceutical properties. These indolocarbazoles are claimed for use in the treatment of CNS diseases, non-insulin-dependent diabetes mellitus, acute stroke and other **neuro**-traumatic injuries, diabetes mellitus, malignant diseases, diseases caused by malfunctioning of specific signaling pathways and neurodegenerative diseases, such as Alzheimer's disease. Thus, indolocarbazole II (R1 =  $\beta$ -NH<sub>2</sub>, R2 =  $\alpha$ -H, R3 = H) was prepared starting from cyclopentadiene, 4-methoxybenzyl amine, dichloromaleic anhydride, and **indole** via a multistep synthetic sequence which included a reaction of 12,13-dihydro-6-[(4-methoxyphenyl)methyl]-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione with cis-3,5-dibromocyclopentene using NaH in THF to form II (R1R3 = bond, R2 = H) in 90.4% yield. II (R1R3 = bond, R2 = H), which contains the target ring skeleton, further underwent an hydroxylation sequence using BH<sub>2</sub>.THF followed by NaOH and H<sub>2</sub>O<sub>2</sub> to form alc. II (R1 =  $\alpha$ -OH, R2 =  $\beta$ -H, R3 = H), oxidation of the alc. to the corresponding ketone II (R1R2 = O, R3 = H), reaction of the ketone with benzylamine to give N-benzyl amine II (R1 =  $\beta$ -NHCH<sub>2</sub>Ph, R2 =  $\alpha$ -H, R3 = H) and, finally, N-debenzylation to give the desired indolocarbazole II (R1 =  $\beta$ -NH<sub>2</sub>, R2 =  $\alpha$ -H, R3 = H). The prepared indolocarbazoles were assayed for inhibiting the activity of a group of protein kinases consisting of extracellular signal regulated kinase 2 (ERK2), **protein kinase** A (PKA), **protein kinase** C (PKC) and glycogen synthase kinase 3 $\beta$  (GSK3 $\beta$ ).